

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANTS: Elmore, Michael James  
Mauchline, Margaret Lamble  
Minton, Nigel Peter  
Pasechnik, Vladimir Artymovich  
Titball, Richard William
- (ii) TITLE OF INVENTION: Type F Botulinum Toxin and Use Thereof
- (iii) NUMBER OF SEQUENCES: 5
- (iv) CORRESPONDENCE ADDRESS:  
(A) ADDRESSEE: STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.  
(B) STREET: 1100 New York Avenue, NW, Suite 600  
(C) CITY: Washington  
(D) STATE: DC  
(E) COUNTRY: USA  
(F) ZIP: 20005
- (v) COMPUTER READABLE FORM:  
(A) MEDIUM TYPE: Floppy disk  
(B) COMPUTER: IBM PC compatible  
(C) OPERATING SYSTEM: PC-DOS/MS-DOS  
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:  
(A) APPLICATION NUMBER: (To Be Assigned)  
(B) FILING DATE: 12-DEC-1997  
(C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:  
(A) APPLICATION NUMBER: PCT/GB96/01409  
(B) FILING DATE: 12-JUN-1996  
(C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:  
(A) APPLICATION NUMBER: GB 9511909.5  
(B) FILING DATE: 12-JUN-1995  
(C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:  
(A) NAME: Esmond, Robert W.  
(B) REGISTRATION NUMBER: 32,893  
(C) REFERENCE/DOCKET NUMBER: 1581.0200000
- (ix) TELECOMMUNICATION INFORMATION:  
(A) TELEPHONE: 202-371-2600  
(B) TELEFAX: 202-371-2540

(2) INFORMATION FOR SEQ ID NO: 1:

- (i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 431 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu Tyr  
 1 5 10 15  
 Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn Asn  
 20 25 30  
 Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly  
 35 40 45  
 Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser  
 50 55 60  
 Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile Tyr  
 65 70 75 80  
 Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro  
 85 90 95  
 Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile Asp  
 100 105 110  
 Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr Asn  
 115 120 125  
 Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys Leu  
 130 135 140  
 Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn Lys  
 145 150 155 160  
 Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg Ile  
 165 170 175  
 Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu Gly  
 180 185 190  
 Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys Asn  
 195 200 205  
 Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr Glu

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210 215 220

Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp Pro  
 225 230 235 240

Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys Arg  
 245 250 255

Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn  
 260 265 270

Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro  
 275 280 285

Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile  
 290 295 300

Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg  
 305 310 315 320

Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr  
 325 330 335

Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys  
 340 345 350

Leu Ile Arg Thr Ser Asn Ser Asn Asn Ser Leu Gly Gln Ile Ile Val  
 355 360 365

Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn  
 370 375 380

Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala  
 385 390 395 400

Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly  
 405 410 415

Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn  
 420 425 430

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 144 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu Tyr  
1 5 10 15  
Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn Asn  
20 25 30  
Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly  
35 40 45  
Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser  
50 55 60  
Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile Tyr  
65 70 75 80  
Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro  
85 90 95  
Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile Asp  
100 105 110  
Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr Asn  
115 120 125  
Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys Leu  
130 135 140

(2) INFORMATION FOR SEQ ID NO: 3:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 144 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn Lys  
1 5 10 15  
Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg Ile  
20 25 30  
Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu Gly

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35 40 45  
 Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys Asn  
 50 55 60  
 Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr Glu  
 65 70 75 80  
 Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp Pro  
 85 90 95  
 Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys Arg  
 100 105 110  
 Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn  
 115 120 125  
 Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro  
 130 135 140

(2) INFORMATION FOR SEQ ID NO: 4:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 143 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile  
 1 5 10 15  
 Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg  
 20 25 30  
 Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr  
 35 40 45  
 Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys  
 50 55 60  
 Leu Ile Arg Thr Ser Asn Ser Asn Asn Ser Leu Gly Gln Ile Ile Val  
 65 70 75 80  
 Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn

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85 90 95  
Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala  
100 105 110  
Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly  
115 120 125  
Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn  
130 135 140

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1293 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

TCATATACTA ATGATAAAAT TCTAATTTTA TATTTTAATA AATTATATAA AAAAATTAAA 60  
GATAACTCTA TTTTAGATAT GCGATATGAA AATAATAAAT TTATAGATAT CTCTGGATAT 120  
GGTTCAAATA TAAGCATTAA TGGAGATGTA TATATTTATT CAACAAATAG AAATCAATTT 180  
GGAATATATA GTAGTAAGCC TAGTGAAGTT AATATAGCTC AAAATAATGA TATTATATAC 240  
AATGGTAGAT ATCAAAATTT TAGTATTAGT TTCTGGGTAA GGATTCCTAA ATACTTCAAT 300  
AAAGTGAATC TTAATAATGA ATATACTATA ATAGATTGTA TAAGGAATAA TAATTCAGGA 360  
TGGAAAATAT CACTTAATTA TAATAAAATA ATTTGGACTT TACAAGATAC TGCTGGAAAT 420  
AATCAAAAAC TAGTTTTTAA TTATACACAA ATGATTAGTA TATCTGATTA TATAAATAAA 480  
TGGATTTTTG TAACTATTAC TAATAATAGA TTAGGCAATT CTAGAATTTA CATCAATGGA 540  
AATTTAATAG ATGAAAAATC AATTTTGAAT TTAGGTGATA TTCATGTTAG TGATAATATA 600  
TTATTTAAAA TTGTTGGTTG TAATGATACA AGATATGTTG GTATAAGATA TTTTAAAGTT 660  
TTTGATACGG AATTAGGTAA AACAGAAATT GAGACTTTAT ATAGTGATGA GCCAGATCCA 720  
AGTATCTTAA AAGACTTTTG GGGAAATTAT TTGTTATATA ATAAAAGATA TTATTTATTG 780

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AATTTACTAA GAACAGATAA GTCTATTACT CAGAATTCAA ACTTTCTAAA TATTAATCAA 840  
 CAAAGAGGTG TTTATCAGAA ACCAAATATT TTTTCCAACA CTAGATTATA TACAGGAGTA 900  
 GAAGTTATTA TAAGAAAAAA TGGATCTACA GATATATCTA ATACAGATAA TTTTGTTAGA 960  
 AAAAATGATC TGGCATATAT TAATGTAGTA GATCGTGATG TAGAATATCG GCTATATGCT 1020  
 GATATATCAA TTGCAAAACC AGAGAAAATA ATAAAATTAA TAAGAACATC TAATTCAAAC 1080  
 AATAGCTTAG GTCAAATTAT AGTTATGGAT TCAATAGGAA ATAATTGCAC AATGAATTTT 1140  
 CAAAACAATA ATGGGGGCAA TATAGGATTA CTAGGTTTTT ATTCAAATAA TTTGGTTGCT 1200  
 AGTAGTTGGT ATTATAACAA TATACGAAAA AATACTAGCA GTAATGGATG CTTTGGAGT 1260  
 TTTATTCTA AAGAGCATGG ATGGCAAGAA AAC 1293

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1313 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

GGATCCATAT GTCTTACACT AACGACAAAA TCCTGATCCT GTACTTCAAC AAAGTGTACA 60  
 AAAAAATCAA AGACAACTCT ATCCTGGACA TCGGTTACGA AAACAACAAA TTCATCGACA 120  
 TCTCTGGCTA TGGTTCTAAC ATCTCTATCA ACGGTGACGT CTACATCTAC TCTACTAACC 180  
 GCAACCAGTT CGGTATCTAC TCTTCTAAAC CGTCTGAAGT AAACATCGCT CAGAACAACG 240  
 ACATCATCTA CAACGGTCGT TACCAGAACT TCTCTATCTC TTTCTGGGTT CGTATCCCGA 300  
 AATACTTCAA CAAAGTTAAC CTGAACAACG AATACACTAT CATCGACTGC ATCCGTAACA 360  
 ACAACTCTGG TTGGAAAATC TCTCTGAAC ACAACAAAAT CATCTGGACT CTGCAGGACA 420  
 CTGCTGGTAA CAACCAGAAA CTGGTTTTC ACTACACTCA GATGATCTCT ATCTCTGACT 480  
 ACATTAATAA ATGGATCTTC GTTACTATCA CTAACAACCG TCTGGGTAAC TCTCGTATCT 540  
 ACATCAACGG TAACCTGATC GATGAAAAAT CTATCTCTAA CCTGGGTGAC ATCCACGTTT 600

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CTGACAACAT CCTGTTCAAA ATCGTTGGTT GCAACGACAC GCGTTACGTT GGTATCCGTT 660  
ACTTCAAAGT TTTCGACACT GAACTGGGTA AACTGAAAT CGAAACTCTG TACTCTGACG 720  
AACCGGACCC GTCTATCCTG AAAGACTTCT GGGGTAAC TA CTGCTGTAC AACAAACGTT 780  
ACTACCTGCT GAACCTGCTG CGGACTGACA AATCTATCAC TCAGAACTCT AACTTCCTGA 840  
ACATCAACCA GCAGCGTGGT GTTTATCAGA AACCTAATAT CTTCTCTAAC ACTCGTCTGT 900  
ACACTGGTGT TGAAGTTATC ATCCGTAAAA ACGGTTCTAC TGACATCTCT AACACTGACA 960  
ACTTCGTACG TAAAAACGAC CTGGCTTACA TCAACGTTGT TGACCGTGAC GTTGAATACC 1020  
GTCTGTACGC TGACATCTCT ATCGCTAAAC CGGAAAAAAT CATCAAAC TG ATCCGTACTT 1080  
CTAACTCTAA CAACTCTCTG GGTCAGATCA TCGTTATGGA CTCGATCGGT AACAACTGCA 1140  
CTATGAACTT CCAGAACAAC AACGGTGGTA ACATCGGTCT GCTGGGTTTC CACTCTAACA 1200  
ACCTGGTTGC TTCTTCTTGG TACTACAACA ACATCCGTAA AAACACTTCT TCTAACGGTT 1260  
GCTTCTGGTC TTTCATCTCT AAAGAACACG GTTGGCAGGA AACTAATCT AGA 1313

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ABSTRACT

The present invention relates to a polypeptide free of toxin activity which gives protection against botulinum type F toxin. The invention also relates to a fusion protein comprising a fragment of a toxin molecule and a purification moiety which enables purification of the fragment from solution. The invention also relates to pharmaceutical compositions comprising the polypeptide or the fusion protein, vaccines comprising the polypeptide, methods of producing the present polypeptides, vaccines and pharmaceutical compositions, and methods of vaccinating a mammal against a botulinum toxin.

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